UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,905	02/14/2002	Ze'ev Ronai	2420/11249US2	1884

7590 09/09/2005

DARBY & DARBY P.C.
805 Third Avenue
New York, NY 10022

EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,905	RONAI, ZE'EV	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005 and 21 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 6-44* is/are pending in the application.

4a) Of the above claim(s) *16-19,22 and 30-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6-15,20,21,23-29 and 33-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20050422*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice of Non-Compliant Amendment.

DETAILED ACTION

1. The supplemental amendment filed June 21, 2005 is acknowledged and has been entered. Claims 2 and 5 have been canceled. Claims 1, 3, 4, 6, 7, and 14 have been amended. Claims 33-44 have been added.

2. Claims 1, 3, 4, and 6-44 are pending in the application. Claims 16-19, 22, and 30-32 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 1, 3, 4, 6-15, 20, 21, 23-29, and 33-44 are currently under prosecution.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The following Office action contains NEW GROUNDS of rejection necessitated by amendment.

Election/Restrictions

6. Upon cancellation of claim 5 and amendment of claims 6 and 7 to depend from claims 1 and 6, respectively, claims 6 and 7 are directed to the subject matter of the elected invention. Accordingly, claims 6 and 7 have been rejoined with the other claims drawn to the elected invention and are currently under examination.

Information Disclosure Statement

7. The information disclosure filed April 22, 2005 has been considered. An initialed copy is enclosed.

Response to Amendment

8. The amendment filed on March 26, 2005 is considered non-compliant because it fails to meet the requirements of 37 CFR § 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). In order for the amendment to be compliant, correction of the following item(s) is required. **Only the corrected section of the non-compliant amendment must be resubmitted (in its entirety), e.g., the entire "Amendments to the specification" section of applicant's amendment must be re-submitted.** 37 CFR § 1.121(h).

As noted on the attached Notice of Non-Compliant Amendment, the amended paragraphs do not include markings showing the changes that have been made relative to the immediate prior versions.

Nevertheless, in order to advance prosecution and in lieu of mailing yet another Notice of Non-Compliant Amendment, the objections to the specification set forth in the Office action mailed December 20, 2004 have been maintained herein for the reasons of record.

For clarity, the amendment filed March 26, 2004 is non-compliant and therefore the amendment to the specification filed March 21, 2005 has not been entered.

Grounds of Objection and Rejection Withdrawn

9. Unless specifically reiterated below, Applicant's amendment and/or arguments have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed December 20, 2004.

Grounds of Objection and Rejection Maintained

Objections to the Specification

10. The objection to the specification set forth in section 8 of the Office action mailed December 20, 2004 is maintained.

As explained, the disclosure is objected to because the disclosure refers to embedded hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified. Reference to hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified is impermissible and therefore requires deletion.

An example of such a disclosure appears in the specification at page 64, line 1.

The attempt to incorporate essential or non-essential subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I regarding acceptable incorporation by reference. See 37 CFR § 1.57.

11. The objection to the specification set forth in section 9 of the Office action mailed December 20, 2004 is maintained.

As explained, the specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

The following are the examples of such improperly demarcated trademarks, which were listed in the previous Office action: include Adriamycin™ (page 39, line 10), CellQuest™ (page 40, line 11), and GenePix™ (page 63, line 27).

In addition to those examples, it is noted that there are additional incidences in which trademarks in the specification are not properly demarcated, such as Taxol™ (page 29, line 6).

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

12. The objection to the specification set forth in section 10 of the Office action mailed December 20, 2004 is maintained.

As explained, the specification is objected to because of the following informality:

"Clontech" is misspelled as "Clonetech" at page 17, line 16.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

13. The rejection of claims 1, 8-13, 15, 20, 21, 23-29, and 33 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement (Federal Register; Vol. 66, No.

4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

The ground of rejection is set forth in section 15 of the Office action mailed December 20, 2004.

At pages 16-19 of the amendment filed March 21, 2005 Applicant has traversed this ground of rejection.

Applicant's arguments traversing this ground of rejection have been carefully considered but not found persuasive for the following reasons:

Although claim 1, as amended, is directed to recite the method comprises inhibiting transcriptional activity of ATF2 by contacting the cell with an agent consisting of at least one of a polypeptide comprising an inhibitory N-terminal fragment of ATF2, an *ATF2* antisense oligonucleotide, an *ATF2* ribozyme, an anti-ATF2 antibody, or an expression vector encoding the ATF2 N-terminal antagonist fragment, the elected invention is the method comprising contacting a tumor cell with a composition comprising a polypeptide. Inasmuch as claim 1 is now directed to a method comprising inhibiting transcriptional activity of ATF2 by contacting the cell with an agent consisting of at least one of a polypeptide comprising an inhibitory N-terminal fragment of ATF2, the issues set forth at page 5, paragraph 6, through page 6, paragraph 1, of the preceding Office action mailed December 20, 2004 have been remedied.

The remaining ground of rejection, however, set forth beginning at page 6, paragraph 2 has not been overcome.

At page 17 of the amendment Applicant addresses the Office's position that the description of 4 N-terminal fragments of ATF2, not all of which inhibit the activity of ATF2, is not representative or adequately descriptive of the genus of fragments of ATF2 to which the claims are directed. In apparent response to this position Applicant has remarked that claim 1, as amended, is directed to "an **inhibitory** N-terminal ATF2 fragment", which is defined by specification at page 9, lines 22-27. Inasmuch as it was already appreciated that the claims 2, 13, 15, 20, 21, and 23-29 were directed to "an N-terminal antagonist fragment of ATF2"

or "an inhibitory ATF2 N-terminal fragment", the fact that claim 1 is now also directed to such a fragment does not serve to resolve the issues set forth in the rejection at page 6, paragraph 2, through page 9 of the Office action mailed December 20, 2004.

At page 18 Applicant has questioned the relevance or relatedness of the *Lilly* decision to the instant inquiry as to whether the disclosure of the claimed invention satisfies the written description requirement set forth under 35 U.S.C. § 112, first paragraph. The Federal Circuit has perhaps best answered this question.

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568). As discussed in greater detail in the preceding Office action mailed December 20, 2004, there is in fact such unpredictability, since unless the polypeptide comprises a fragment of ATF2 that comprises the p38 and JNK phosphorylation sites, it cannot be predicted whether the polypeptide is capable of inhibiting the growth of a tumor cell in the manner of Peptide II (amino acids 50-100 of ATF2), which is described in this instance.

As the claims encompass the use of polypeptides comprising N-terminal fragments of ATF2 to inhibit the growth of a tumor cell and/or treat cancer, it is duly noted that apart from a peptide comprising amino acids 50-100 of ATF2, which contain the p38 and JNK phosphorylation sites, the supporting disclosure does not describe other polypeptides comprising an N-terminal fragment of ATF2 that are capable of inhibiting the growth of a tumor. "[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, as in that, there is no language that adequately describes inhibitory N-terminal fragments of ATF2 that can be used to inhibit the growth of a tumor or to

achieve the claimed therapeutic effect. A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

Recognizing again that the claims are drawn to a method for inhibiting the growth of a tumor cell or treating a tumor in a subject comprising contacting the tumor cell or administering to a subject a polypeptide comprising an inhibitory N-terminal fragment of ATF2, it is aptly noted that the Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability to inhibit an activity of BMP-2 to achieve therapeutic effect, does not provide an adequate written description of the genus. See *The Reagents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). Once again, the recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Although *Lilly* related to claims drawn to genetic material, the statute applies to all types of inventions. "Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1894 (CAFC 2004). The claimed method depends upon finding a polypeptide comprising an inhibitory N-terminal fragment of ATF2 that has the ability to inhibit the growth of a tumor cell to achieve therapeutic effect in treating cancer using the claimed process; without an agent comprising such a polypeptide, it is impossible to practice the invention.

In addition, although the skilled artisan could potentially identify such agents that might be used in practicing the claimed invention by screening for polypeptides comprising an inhibitory N-terminal fragment of ATF2 that has the ability to inhibit the growth of a tumor cell to achieve therapeutic effect in treating

cancer, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Absent the adequate description of a representative number of members of the genus of agents comprising polypeptides comprising an inhibitory N-terminal fragment of ATF2 that has the ability to inhibit the growth of a tumor cell, the supporting disclosure amounts to no more than a mere invitation to identify such agents that can be used in processes for inhibiting the growth of tumor cells and treating cancer.

Finally, Applicant is again directed to refer to the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001), which explains that possession may be shown in a variety of ways, but in this instance, because the claims encompass a genus of substances having the ability to inhibit an activity of ATF2 to achieve therapeutic effect in the treatment of cancer, which vary both structurally and functionally, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. These guidelines have been written in light of the guidance on this issue provided by the Courts over the past many

years. Again, it is submitted that here Applicant's disclosure of the claimed invention fails to satisfy the written description requirement, since factual evidence of an actual reduction to practice has not been disclosed in the specification; Applicant's specification has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant's specification has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

Nevertheless, at page 18 of the amendment Applicant has asserted that the *Lilly* decision is not relevant to the instant inquiry, since in this case the amino acid sequence of the N-terminus of ATF2 is already known. Agreeably, the entire amino acid sequence, including its arbitrarily defined N-terminus, was known at the time the application was filed; notably, however, the claims are not directed to polypeptides of known sequence and structure but rather to polypeptides, which comprise fragments of the known amino acid sequence of ATF2 possessing the ability to inhibit the growth of a tumor cell. As the record shows, while the prior art teaches N-terminal fragments of ATF2 that are capable of inhibiting the growth of a tumor cell, the claims are not directed solely to such fragments but are instead directed to a genus of structurally varying polypeptides comprising an inhibitory N-terminal fragment of ATF2.

Then, beginning at page 18, paragraph 5, of the amendment Applicant has asserted that it is erroneous to interpret the specification as describing only peptides containing the region comprising the p38 and JNK phosphorylation sites (amino acids 69 and 71) as inhibitory, such as "Peptide II", which consists of amino acids 50-100 of ATF2. Applicant has based this assertion upon the contention that the specification teaches "Peptide IV" (amino acids 150-200 of ATF2), which lacks amino acids 69 and 71, has inhibitory activity in combination with chemotherapeutics. However, as noted at page 7, paragraph 2, of the Office action mailed December 20, 2004, the specification teaches that Peptide IV increased resistance of melanoma cells to UV- and drug-induced apoptosis

(see, e.g., page 50, lines 22-24) and accordingly teaches that only Peptide II efficiently increased sensitivity of tumor cells to the cytotoxic effects of UV-irradiation and treatments with chemotherapeutic agents (see, e.g., page 49, lines 13-19).

Applicant further alleges that additional rebuttal evidence of the erroneous nature of this interpretation is found in a commonly owned application recently filed, which purportedly describes a 10 amino acid inhibitory fragment of ATF2 that lacks amino acids 69 and 71 of ATF2. If indeed Applicant's additional rebuttal evidence were to be demonstrate that fragments lacking amino acids 69 and 71 are inhibitory and therefore encompassed by the claims, then it is submitted that there is no particularly identifying (i.e., substantial) structural feature (e.g., amino acids 69 and 71, which are the p38 and JNK phosphorylation sites) common among members of the genus of inhibitory N-terminal fragments of ATF2 to which the claims are directed that is disclosed in the specification that correlates with their common ability to inhibit the growth of a tumor cell. If indeed no such correlation is described in the specification, then it is submitted that the disclosure of the claimed invention would not permit the skilled artisan to immediately envision, recognize or distinguish at least a substantial number of the members of the genus of polypeptides comprising such inhibitory N-terminal fragments of ATF2 to which the claims are directed. Accordingly, the specification cannot be considered to reasonably convey to skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 102

14. The rejection of claims 1, 3, 4, 6-10, 12-14, 20, 23-26, 29, 33-39, 43, and 44 under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,579,856 B2, as evidenced by van Dam et al. (*EMBO J.* 1995 Apr 18; **14** (8): 1798-1811), is maintained, as further evidenced by Bhoumik et al. (*Proc. Natl. Acad. Sci. USA.* 2004 Mar 23; **101** (12): 4222-4227) (of record).

In order to advance prosecution, it has been presumed that claim 34 should properly depend from claim 33.

The ground of rejection is set forth in section 18 of the Office action mailed December 20, 2004.

At pages 20 and 21 of the amendment filed March 21, 2005 Applicant has traversed this ground of rejection.

Applicant's arguments traversing this ground of rejection have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that prior art fails to anticipate the claimed invention, since, as amended, the claims are directed to an agent comprising a polypeptide comprising an inhibitory N-terminal fragment of ATF2, which excludes full-length ATF2. In reply, it is true that the specification expressly excludes "full-length ATF2" from the meaning of the term "inhibitory ATF2 N-terminal fragment" (page 9, lines 18-20), as noted in the previous Office action at page 6. Nevertheless, the dominant negative mutant that is disclosed by the prior art is not full-length ATF2; rather, it is a polypeptide comprising an inhibitory N-terminal fragment of ATF2.

Moreover, as set forth at page 13 of the previous Office action, the prior art teaches a method for treating a tumor in a subject by increasing the sensitivity of the tumor cells to a cancer therapy by contacting the tumor cells with a dominant negative mutant of ATF2 comprising the minimal transactivation domain at the amino-terminus of ATF2; see entire document (e.g., the abstract; column 6, lines 27-47; column 12, lines 5-31; column 13, lines 53-55; column 15, lines 53-62; claims 5 and 8). The prior art teaches the dominant negative mutant of ATF2 is prepared according to the teachings of van Dam et al. (*EMBO J.* 1995 Apr 18; **14** (8): 1798-1811); see column 12, lines 18-21. van Dam et al. teaches a dominant negative mutant of ATF2 comprising the minimal transactivation domain at the amino-terminus of ATF2, which comprises amino acids 19-96 of ATF2; see entire document (e.g., page 1809, column 2). The prior art teaches the disclosed process comprises inhibiting transcription regulated by ATF2; see,

e.g., column 6, lines 59-66. Thus, absent a showing of any difference, the prior art teaches a polypeptide that is deemed the same as the polypeptide to which the clams are directed, since van Dam et al. teaches a polypeptide comprising an inhibitory ATF2 N-terminal fragment having a sequence consisting of from about amino acid 50 to about amino acid 100 of ATF2, which when used in the process of treating a tumor inhibits the growth of that tumor and inhibits the transcriptional activity of ATF2.

Notably the Office does not have the facilities for examining and comparing the product to which the instant claims are directed with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the other. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the polypeptide to which the claims are directed is different than the polypeptide that is taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

With regard to claims 35-39, 43, and 44, notably the prior art does not actually teach the inhibitory N-terminal fragment of which the disclosed polypeptide is comprised increases the activity of a c-jun family member, or more particularly the activity of jun kinase (JNK). Nevertheless, as evidenced by Bhoumik et al., a polypeptide comprising an N-terminal fragment of ATF2 binds to JNK and increases its activity (abstract). Given that the composition comprising the polypeptide of the prior art, which is administered to a subject to treat cancer, inhibits the transcriptional activity of ATF2 and inhibits the growth of a tumor cell, cannot be materially or structurally distinguished from the agent comprising a polypeptide to which the claims are directed, the polypeptide of the prior art is deemed the same as the polypeptide to which the claims are directed, which increases the activity of JNK, as its ability to do so in an inherent property of that polypeptide.

As evidence that such an activity is an inherent property of a polypeptide comprising an inhibitory N-terminal fragment of ATF2, Bhoumik et al. teaches a polypeptide comprising an inhibitory N-terminal fragment of ATF2 (amino acids 50-100 of ATF2) binds to JNK and increases its activity; see entire document (e.g., the abstract).

Although it was perhaps not appreciated that the polypeptide disclosed by the prior art increases the activity of JNK, Applicant is reminded that the claims are directed to a polypeptide that inhibits the growth of a tumor cell comprising inhibiting the transcriptional activity of ATF2 and the mechanism of action does not have a bearing on the patentability of the invention, if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. See *In re Wiseman,* 201 USPQ 658 (CCPA 1979). Furthermore, granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. See *In re Baxter Travenol Labs,* 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP § 2145. The Court of Appeals for the Federal Circuit has stated that "[I]t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable" See *In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1575, 1936 (Fed. Cir. 1990) (emphasis in original). See also *Bristol-Myers Squibb Company v. Ben Venue Laboratories*, 58 USPQ2d 1508 (CAFC 2001) at 1514: "Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent". As to inherency, the Court has noted that "[u]nder the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates." *Mehl/Biophile Int'l Corp. v. Miligraum*, 192 F.2d 1362, 1366, 52 USPQ2d 1303, 1305 (Fed. Cir. 1999) (citations omitted). Moreover, "[w]here [...] the result is necessary consequence of what was deliberately intended, it is no import that the article's authors did not appreciate the results." *Mehl/Biophile Int'l Corp*, 192 F.2d 1362, 52 USPQ2d at 1307.

With further regard to claim 44, the prior art does not expressly teach that administering the disclosed polypeptide comprising the N-terminal fragment of ATF2 inhibits the metastasis of melanoma cells. Nevertheless, if the treatment inhibits the growth of melanoma cells, it necessarily also inhibits the metastasis of those cells.

As evidence that the process disclosed by the prior art inherently inhibits metastasis of melanoma cells, Bhoumik et al. teaches that administering a polypeptide comprising an inhibitory N-terminal fragment of ATF2 (amino acids 50-100 of ATF2) to a subject results in inhibition of melanoma tumorigenicity and metastatic potential *in vivo* (page 4222, paragraph bridging columns 1 and 2). Again, if the treatment disclosed by the prior art inhibits the growth of melanoma cells, and it also results in inhibition of melanoma tumorigenicity and metastatic potential *in vivo*, it inhibits the metastasis of those cells.

Finally, it is noted that at page 21 of the amendment Applicant has remarked that the claims "were also rejected over the van Dam reference alone" (amendment filed March 21, 2005, page 21, paragraph 1). To the contrary, van Dam et al. is cited as an evidentiary reference only; none of the claims were rejected over this reference alone. See MPEP §§ 2112, 2124, and 2131.01.

Claim Rejections - 35 USC § 103

15. The rejection of claims 1, 10, 11, 23, 26-28, 40, and 41 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,579,856 B2, as evidenced by van Dam et al. (*EMBO J.* 1995 Apr 18; **14** (8): 1798-1811), in view of Ivanov et al. (*Oncogene*. 2000; **19**: 3003-3012), is maintained.

In order to advance prosecution, it has been presumed that claim 34 should depend from claim 33.

Claim 1, 10, 11, 40, and 41 are drawn to a method for inhibiting the growth of a tumor cell comprising inhibiting the transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ATF2 and further treating the tumor cell with the chemotherapeutic agent SB203580. Claims 23

and 26-28 are drawn to a method for treating a tumor in a subject comprising administering a composition comprising a polypeptide comprising an inhibitory ATF-2 N-terminal fragment and further treating the tumor with the p38 inhibitor SB203580.

The ground of rejection is set forth in section 20 of the Office action mailed December 20, 2004.

At pages 21-23 of the amendment filed March 21, 2005 Applicant has traversed this ground of rejection.

Applicant's arguments traversing this ground of rejection have been carefully considered but not found persuasive for the following reasons:

At page 22 of the amendment Applicant has asserted that prior art does not teach an agent comprising a polypeptide comprising an inhibitory N-terminal fragment of ATF2. The merit of this argument has been addressed above in responding to Applicant's traversal of the rejection under 35 U.S.C. § 102. Because, absent a showing of any difference, the prior art teaches a polypeptide that is deemed the same as the polypeptide to which the clams are directed, most of the arguments that follow this errant assertion are moot.

Applicant has argued that the prior art does not teach or suggest inhibiting the growth of a tumor cell by a process comprising inhibiting the transcriptional activity of ATF2 by contacting the cell with an agent comprising an *ATF2* antisense oligonucleotide, an *ATF2* ribozyme, an anti-ATF2 antibody, or an expression vector encoding an ATF2 N-terminal antagonist fragment. This argument is not relevant to the instant ground of rejection, however, since only claims drawn to the elected invention are currently under prosecution.

Applicant has argued that neither reference teaches the use of the inhibitory N-terminal ATF2 peptides to sensitize cancer cells to radiation. To the contrary, as noted in the preceding Office action, '856 teaches the process comprises radiotherapy and/or chemotherapy, as '856 teaches that, in order to improve therapeutic advantage, therapies are often used in combination; see, e.g., column 2, lines 56-65; and column 16, lines 24-29. Moreover, '856 teaches

that the process allows a lower dose of a conventional therapeutic modality, such as radiation or chemotherapy, to be used; see, e.g., column 16, lines 24-29. The fact that the process allows a lower dose of a conventional therapeutic modality, such as radiation, suggests the use of the inhibitory N-terminal ATF2 peptides to sensitize cancer cells to radiation. Nevertheless, it is duly noted that In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the use of the inhibitory N-terminal ATF2 peptides to sensitize cancer cells to radiation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). At present, claim 12, for example, merely recites the method of claim 1, further comprising treating the tumor cell with radiation; there is no recitation in the claims that the further treatment of the cell with radiation achieves sensitization of the cell to the cytotoxic or cytostatic effects of the radiation.

Applicant has asserted that the present invention "unexpectedly demonstrates that ATF2 inhibitory peptides [that] **do not** affect phosphorylation of residues 69 and 71 also inhibit ATF2 activity" (emphasis in the original; amendment filed March 21, 2005, page 22, paragraph 4), which Applicant argues "is in contrast to the prior art teachings that these any inhibitor must abrogate phosphorylation of these residues [sic]" (paragraph bridging pages 22 and 23). While difficult to interpret Applicant's argument, it is believed that the prior art teaches an agent comprising a polypeptide comprising an inhibitory N-terminal fragment of ATF2 that cannot be materially or structurally distinguished from the polypeptide to which the claims are directed. Therefore, it is not pertinent that Applicant found unexpectedly that the fragments of ATF2, which do not comprise amino acids 69 and 71, are capable of inhibiting the activity of ATF2, since the claims are directed to inhibitory N-terminal fragments of ATF2 that comprise these amino acids.

Finally, in response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, as set forth in the preceding Office action, it would have been obvious to one ordinarily skilled in the art at the time of the invention to have treated tumor cells by a process comprising administering to a patient having a tumor a composition comprising a dominant negative mutant of ATF2, according to '856, and further treating the tumor by administering to the patient an effective dose of SB203580 to sensitize the tumor cells to UV-irradiation, because '856 teaches, in order to improve therapeutic advantage, therapies are often used in combination, and moreover because '856 teaches a dominant negative mutant of ATF2 sensitizes tumor cells to radiotherapy, whereas Ivanov et al. teaches SB203580 sensitizes tumor cells to radiotherapy. Therefore, one ordinarily skilled in the art at the time of the invention would have been motivated to do so to treat a tumor with an improved therapeutic advantage. Furthermore, one ordinarily skilled in the art at the time of the invention would have had a reasonable expectation of success in doing so, since the prior art teaches that both the mutant protein and SB203580 sensitize tumor cells to the cytotoxic effects of irradiation.

16. The rejection of claims 13, 15, 21, 23-26, and 29 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,579,856 B2, as evidenced by van Dam et al. (*EMBO J.* 1995 Apr 18; **14** (8): 1798-1811), in view of US Patent No. 6,335,178 B1, is maintained.

The ground of rejection is set forth in section 21 of the Office action mailed December 20, 2004.

It appears that Applicant has intended the traversal of the above rejection of claims 1, 10, 11, 23, 26-28, 40, and 41 under 35 U.S.C. 103(a) to serve as the traversal of this ground of rejection, since Applicant has not specifically addressed this ground of rejection in the amendment filed March 21, 2005 or any amendment filed since.

Applicant's arguments traversing this and the above ground of rejection have been carefully considered but not found persuasive for the reasons provided above.

17. The rejection of claims 27 and 28 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,579,856 B2, as evidenced by van Dam et al. (*EMBO J.* 1995 Apr 18; **14** (8): 1798-1811), in view of US Patent No. 6,335,178, as applied to claim 13, 15, 21, 23-26, and 29 above, and further in view of Ivanov et al. (*Oncogene*. 2000; **19**: 3003-3012), is maintained.

The ground of rejection is set forth in section 22 of the Office action mailed December 20, 2004.

It appears that Applicant has intended the traversal of the above rejection of claims 1, 10, 11, 23, 26-28, 40, and 41 under 35 U.S.C. 103(a) to serve as the traversal of this ground of rejection, since Applicant has not specifically addressed this ground of rejection in the amendment filed March 21, 2005 or any amendment filed since.

Applicant's arguments traversing this and the above ground of rejection have been carefully considered but not found persuasive for the reasons provided above.

New Grounds of Objection

Claim Objections

18. Claim 1 is objected to because it is directed to a method comprising "inhibiting transcriptional activity of ATF2 by contacting the cell with an agent consisting of at least one of a polypeptide comprising an inhibitory N-terminal

fragment of ATF2, an *ATF2* antisense oligonucleotide, an *ATF2* ribozyme, an anti-ATF2 antibody, or an expression vector encoding the ATF2 N-terminal antagonist fragment. If the agent consists *of at least one* of the products recited in the claim, the claim should read, "an agent consisting of at least one of a polypeptide comprising an inhibitory N-terminal fragment of ATF2, an *ATF2* antisense oligonucleotide, an *ATF2* ribozyme, an anti-ATF2 antibody, **and** an expression vector encoding the ATF2 N-terminal antagonist fragment" (emboldened for emphasis). Appropriate correction is required.

19. Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 4 depends from claim 3; therefore, although claim 4 recites the inhibitory N-terminal fragment of ATF2 comprises amino acid residues from about residue 50 of ATF2 to about 75 of ATF2, because it depends from claim 3, the fragment to which claim 4 is directed necessarily comprises amino acid residues from about residue 50 of ATF2 to about 100 of ATF2, as does the fragment to which claim 3 is directed. In other words, a fragment that comprises amino acid residues from about residue 50 of ATF2 to about 100 of ATF2 must also comprise amino acid residues from about residue 50 of ATF2 to about 75 of ATF2. Accordingly, claim 4 does not further limit the subject matter of claim 3.

20. Applicant is advised that should claim 3 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

As explained in section 17 above, claim 4 does not further limit the subject matter of claim 3; therefore, claim 4 is a substantial duplicate of claim 3.

21. Claims 1, 3, 4, 6-12 are objected to as being drawn in the alternative to the subject matter of non-elected inventions. Appropriate correction is required.

22. Claim 35 is objected to because "increases" is mistyped as "increase". The claim should read, "wherein the inhibitory N-terminal fragment increases the activity of a c-jun family member". Appropriate correction is required.

New Grounds of Rejection

23. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

24. Claims 1, 3, 4, 6-12, and 34-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 4, and 6-12 are indefinite because claim 1 recites, "the ATF2 N-terminal antagonist fragment". The limitation is not supported by antecedent basis in the claim and accordingly it is not clear to which ATF2 N-terminal antagonist fragment the claim refers. Therefore, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined in a manner that satisfies the requirements set forth under 35 U.S.C. § 112, second paragraph.

Claim 4 is indefinite because the claim recites, "the inhibitory N-terminal fragment of ATF2 comprises amino acid residues from about residue 50 of ATF2 to about 75 of ATF2". This recitation renders the claim indefinite because the claim depends from claim 3, which recites, "the inhibitory N-terminal fragment of ATF2 comprises amino acid residues from about residue 50 of ATF2 to about 100 of ATF2". A fragment that comprises amino acid residues from about residue 50 of ATF2 to about amino acid residue 100 of ATF2 must necessarily

comprise amino acid residues from about residue 50 of ATF2 to about 75 of ATF2; but a fragment that necessarily comprises amino acid residue 50 of ATF2 to about 100 of ATF2 cannot comprise fewer amino acid residues. For example, such a fragment cannot comprise amino acid residues from about amino acid residue 50 of ATF2 to about amino acid residue 75 of ATF2 *without also comprising amino acid residues from about amino acid residue 75 to about amino acid residue 100 of ATF2.* For this reason, it cannot be determined if the subject matter regarded as the invention of claim 4 excludes a fragment comprising amino acid residues from about amino acid residue 75 of ATF2 to about amino acid residue 100 of ATF2. Accordingly, claim 4 fails to particularly point out and distinctly claim the subject matter that Applicant regards as the invention, as required by 35 U.S.C. §112, second paragraph, since it fails to clearly delineate that subject matter in a manner that would enable the artisan to recognize infringing subject matter.

This latter issue may be remedied, for example, by amending claim 4 to depend from claim 1, rather than from claim 3.

Claims 34-44 are indefinite because, as claim 34 is presently written, the claim depends from itself. While for the purpose of advancing prosecution, it has been presumed that claim 34 should properly depend from claim 33, as claim 34 is presently written, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined.

Claims 34-44 are indefinite because, as claim 34 presently depends from itself, it is drawn to a method, but fails to recite an active step. Accordingly, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined.

Claims 35-44 are indefinite because claim 35 recites, "wherein the inhibitory N-terminal fragment further increase[s] the activity of a c-jun family member". Although claim 34 is presently improperly dependent upon itself and is thus drawn to a method without steps, it is presumed claim 34 should properly depend from claim 33. If that is indeed the case, then claim 35 should be drawn

to a method of inhibiting growth of a tumor cell comprising inhibiting transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ATF2, which further increases the activity of a c-jun family member. It cannot be determined relative to what reference value of the activity of a c-jun family member or standard the fragment to which the claim is directed is necessarily able to increase the activity of that member. Moreover, since the fragment "further" increases the activity, there is an implication that the process comprises a step that causes an initial increase in that activity, which is then "further" increased by contacting the cell with the fragment. Because the step(s) of which the claimed process is comprised that cause an initial increase in that activity are not recited in the claim, it is not possible to determine whether, or to what extent, contacting the cell with the fragment further increases that level of activity. Accordingly, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined and moreover it would not be possible to determine the subject matter that infringes the claim without first knowing or determining relative to what standard or extent the fragment further increases the activity of c-jun family member.

This latter issue may be remedied, for example, by deleting "further" from the claim, such that the claim would read, "wherein contacting the cell with the inhibitory N-terminal fragment increase[s] the activity of a c-jun family member in the cell, as compared to the activity of the c-jun family member in the cell before it was contacted by the fragment".

Claims 37-44 are indefinite because, as claim 34 presently depends from itself, claims 37, 38, 39, and 43 recite "the tumor cell", which finds no antecedent basis in any of the preceding claims. Accordingly, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined.

Claim 44 is indefinite because it recites, "wherein metastasis of the melanoma cell is *further* inhibited" (italics added for emphasis). As explained above, it is presumed claim 34 should properly depend from claim 33. If that is indeed the case, then claim 44 should be drawn to a method of inhibiting growth

of a melanoma tumor cell comprising inhibiting transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ATF2, wherein metastasis of the melanoma cell is further inhibited. Since the claimed process "further" inhibits metastasis of the melanoma cell, there is an implication that the process comprises a step that causes an initial inhibition of the metastasis of the cell, which is then "further" inhibited by contacting the cell with the fragment. The standard by which the further inhibition (i.e., increased inhibition) is measured is not recited in the claim nor can be ascertained. Furthermore, because the step(s) of which the claimed process is comprised that cause an initial inhibition of the metastasis of the cell are not recited in the claim, it is not possible to determine whether, or to what extent, contacting the cell with the fragment further increases that inhibition. Accordingly, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined and moreover it would not be possible to determine the subject matter that infringes the claim without first knowing or determining relative to what standard or extent the fragment further inhibits metastasis of the cell.

This latter issue may be remedied, for example, by amending claim 44 to recite, "whereby contacting the cell with the inhibitory N-terminal fragment of ATF2 inhibits its metastasis".

25. Claims 1, 3, 4, and 6-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "new matter" rejection.

Claim 1, as amended, is directed to a method comprising "inhibiting transcriptional activity of ATF2 by contacting the cell with **an agent consisting of at least one of** a polypeptide comprising an inhibitory N-terminal fragment of ATF2, an *ATF2* antisense oligonucleotide, an *ATF2* ribozyme, an anti-ATF2

antibody, or [sic] an expression vector encoding the ATF2 N-terminal antagonist fragment" (emboldened for emphasis).

At page 16 of the amendment filed March 21, 2005 Applicant has asserted that support for the amendment to claim 1 is found in the specification, including the claims, as originally filed, at page 9, lines 22-27, page 10, and pages 22 through page 23.

The specification teaches, for example, ATF2 inhibition provides first or second (or later) line approach to cancer therapy, and can be used alone or preferably in combination with a traditional therapeutic approach, e.g., chemotherapy or radiation. However, the specification, including the claims, as originally filed, and more particularly those particular disclosures to which Applicant has referred, do not appear to provide written support for a method for inhibiting the growth of tumor cells or treating cancer comprising inhibiting transcriptional activity of ATF2 by contacting the cell with *an agent consisting of at least one of* any of the non-traditional therapeutic modalities recited in the claim.

The specification would provide the necessary written support were claim 1 to be amended to read, for example, "comprising inhibiting transcriptional activity of ATF2 by contacting the cell with a pharmaceutical composition comprising an agent selected from the group consisting of an inhibitory N-terminal fragment of ATF2, an *ATF2* antisense oligonucleotide, an *ATF2* ribozyme, an anti-ATF2 antibody, and an expression vector encoding an ATF2 N-terminal antagonist fragment".

Accordingly, this issue may be remedied by amending claim 1, as has been suggested in the paragraph above, or otherwise by pointing to particular disclosures in the specification, including the claims, as originally filed, that are believed to provide written support for the present claim language.

Conclusion

26. No claim is allowed.

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
August 22, 2005

Notice of Non-Compliant Amendment (37 CFR 1.121)	Application No. 10/076,905	Applicant(s) RONAI, ZE'EV	
	Examiner Stephen L. Rawlings, Ph.D.	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

The amendment document filed on *21 March 2005* is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121. In order for the amendment document to be compliant, correction of the following item(s) is required.

THE FOLLOWING MARKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

- ☒ 1. Amendments to the specification:
  - ☒ A. Amended paragraph(s) do not include markings.
  - ☐ B. New paragraph(s) should not be underlined.
  - ☐ C. Other _____.
- ☐ 2. Abstract:
  - ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
  - ☐ B. Other _____.
- ☐ 3. Amendments to the drawings:
  - ☐ A. The drawings are not properly identified in the top margin as "Replacement Sheet," "New Sheet," or "Annotated Sheet" as required by 37 CFR 1.121(d).
  - ☐ B. The practice of submitting proposed drawing correction has been eliminated. Replacement drawings showing amended figures, without markings, in compliance with 37 CFR 1.84 are required.
  - ☐ C. Other _____.
- ☐ 4. Amendments to the claims:
  - ☐ A. A complete listing of all of the claims is not present.
  - ☐ B. The listing of claims does not include the text of all pending claims (including withdrawn claims)
  - ☐ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by using one of the following status identifiers: (Original), (Currently amended), (Canceled), (Previously presented), (New), (Not entered), (Withdrawn) and (Withdrawn-currently amended).
  - ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
  - ☐ E. Other: _____.

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP § 714 and the USPTO website at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officeflyer.pdf .

TIME PERIODS FOR FILING A REPLY TO THIS NOTICE:

1. Applicant is given **no new time period** if the non-compliant amendment is an after-final amendment or an amendment filed after allowance. If applicant wishes to resubmit the non-compliant after-final amendment with corrections, the **entire corrected amendment** must be resubmitted within the time period set forth in the final Office action.

2. Applicant is given **one month**, or thirty (30) days, whichever is longer, from the mail date of this notice to supply the **corrected section** of the non-compliant amendment in compliance with 37 CFR 1.121, if the non-compliant amendment is one of the following: a preliminary amendment, a non-final amendment (including a submission for a request for continued examination (RCE) under 37 CFR 1.114), a supplemental amendment filed within a suspension period under 37 CFR 1.103(a) or (c), and an amendment filed in response to a *Quayle* action.

   Extensions of time are available under 37 CFR 1.136(a) only if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action.

   Failure to timely respond to this notice will result in:
   Abandonment of the application if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action; or
   Non-entry of the amendment if the non-compliant amendment is a preliminary amendment or supplemental amendment.